

Remarks

Applicants have read and considered the Office Action dated March 15, 2006 and the references cited therein. Applicants thank the Examiner for the careful review of the application. Applicants respectfully request reconsideration of the present case in view of the following remarks.

Claims 1-24 are currently pending. Claims 25-27 are withdrawn. Claims 1, 3, 5, 9-11, 16-19, and 24-26 are amended. Claim 2 has been cancelled. Amendments to claims 1 and 19 are supported by original claims 2-3, 24, and throughout the specification. In particular, support is found at page 18, third paragraph to page 19, second paragraph, where the mechanism of RNA isolation is expressly specified as precipitation, and the polymeric membrane is described as playing a passive role, acting as a physical barrier to the precipitate. Amendment to claim 5 is supported at page 16, line 1. Amendments to claims 16-18 are supported at least at page 21. With the above additions and amendments to the claims, no new matter has been added.

Preliminary Amendments

Applicants thank the Examiner for the acknowledgement of the preliminary amendment for correction of Tables 3 and 4.

A preliminary amendment submitted to the Office for the present application on 26 November 2003, was instead assigned to Application Serial No. 10/631,189. The subject matter of the preliminary amendment is represented herein for the Examiner's consideration. A copy of the originally filed preliminary amendment is attached herewith as evidence Applicant's request for priority was timely presented.

Interview Summary

On June 14, 2006, a telephonic interview was conducted by Mark Skoog and Hema Viswanathan with Examiner Crow and Primary Examiner B.J. Forman. The subject matter of the invention was discussed. Specifically, it was agreed that the prior art cited in the present rejections described the use of affinity chromatography to separate nucleic acids. In contrast, the presently claimed methods use precipitation of RNA on a polymeric membrane to effect separation, with the polymeric membrane acting as a physical barrier to the precipitate.

Applicants thank Examiners for their time and consideration.

Rejections under 35 U.S.C. §112

Claims 1-24 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The indicated language in claims, 1, 3, 10, 16, 19, and 24 has been clarified by amendment. These amendments are made without prejudice or disclaimer. No subject matter has been surrendered. A summary of the corrections and clarifications follow.

Claims 1 and 19 are amended to remove the tissue/cell lysate language and the claims as amended recite lysate generally. A similar clarification was also made in claims 9 and 10. At the Examiner's request, abbreviations for "gDNA" and various polymers, e.g., "PVP" have been replaced with their full names. In claim 10, "alike" has been removed. In claim 16, the wash buffers have been replaced by the term "wash solution" and by content.

In view of these amendments, Applicants request the rejections for indefiniteness be removed.

Rejections under 35 U.S.C. §102

Claims 1, 2, 5, 6, 9, 10, 12, 14, 15, 16, and 18 are rejected as anticipated by Sambrook et al. *Molecular Cloning. A Laboratory Manual*, 2nd Ed., pages 7.12-7.15 and 7.26-7.29. Applicants respectfully traverse.

Independent claims 1 and 19, as amended, are directed to methods for preparing an RNA sample free of genomic DNA, wherein at least one step involves contacting an RNA isolation membrane with an RNA-containing precipitate. As claimed, the membrane is a polymeric membrane that acts as a physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification. The claims, as amended, are expressly supported by the description in the Specification, at page 18, third paragraph to page 19, first paragraph, which provides:

The mechanism of RNA isolation is via precipitation. RNA, either in a purified or semi-purified (following prefiltration) form or in a complex biological sample, will precipitate in the presence of guanidine and

ethanol. This precipitate can be collected via, for example, centrifugation. The RNA isolation membrane column of the present invention facilitates the collection of the RNA precipitate, washing of the collected precipitate (reduced wash volumes and centrifugation times) and resuspension and elution of the target nucleic acid.

Although the membrane material plays a passive role, acting as a physical barrier to the precipitate, the nature of the polymeric material is important for efficient precipitate collection and to reduce absorptive losses. For example, comparison of various pore sizes of membranes results in changes in the mass recovery of RNA. Similarly, comparison of membranes prepared from different polymeric constituents also varies the mass recovery of RNA. (emphasis added).

In contrast, Sambrook discloses a method for isolating poly(A)+ RNA from previously purified total cytoplasmic RNA by affinity chromatography, using oligo(dT)-cellulose membranes as affinity columns. This is not the same as the method for RNA isolation recited in claim 1, where the polymeric membrane used to separate RNA plays a passive role and acts as a physical barrier to the precipitate that retains the precipitate for purification, rather than as an affinity chromatography column.

The polymeric membranes of the present claims are not described as being specially derivatized with nucleic acid moieties or other molecules for increasing RNA-binding affinity. In fact, the disclosure teaches that the nature of the polymeric material of the membrane is selected to reduce absorptive losses of RNA. (Specification, page 19).

For at least the above reasons, Sambrook et al. does not teach all the limitations of claim 1. Claims 2, 5, 6, 9, 10, 12, 14, 15, 16, and 18 depend from claim 1, and therefore include the limitations of claim 1 and parallel reasoning. In view of the amendment to claim 1 and comments provided, Applicants request withdrawal of the rejection and reconsideration of claims 1, 2, 5, 6, 9, 10, 12, 14, 15, 16, and 18.

Rejections under 35 U.S.C. §103

1. Claims 1–2, 4–10, 12–21 and 23 are rejected under 35 U.S.C. §103 as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook. Applicants respectfully disagree.

Independent claims 1 and 19, as amended, are directed to methods for preparing an RNA sample free of genomic DNA, wherein at least one step involves contacting an RNA isolation membrane with an RNA-containing precipitate. As claimed, the membrane is a polymeric membrane that acts as a physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification.

In contrast, Colpan teaches methods for purification of nucleic acids in general from biological samples, but does not teach or otherwise suggest segregation of specific types of nucleic acids, namely DNA, plasmid or genomic, from RNA. In fact, the Office concedes that Colpan is silent with respect to a second column or membrane used specifically to isolate RNA.

The Office Action employs Sambrook to overcome the shortcomings of Colpan with the disclosure of a column or polymeric membrane used to isolate RNA. Sambrook teaches a derivatized oligo(dT)-cellulose membrane for use as an affinity chromatography column to separate poly(A)+ RNA from total cytoplasmic RNA. Neither Colpan nor Sambrook teaches an RNA isolation method where the mechanism of separation is precipitation, and where the RNA is isolated by means of a polymeric membrane that acts as a physical barrier (rather than an affinity column) for the precipitate, and retains the precipitate on the membrane for purification.

Applicants assert that Sambrook and Colpan, taken alone, or in combination, fail to teach all the limitations of the present claims. Therefore, the Examiner has not established a *prima facie* case of obviousness and the Applicants respectfully request withdrawal of the rejection and reconsideration of the claims in view of the amendments to the claims and remarks presented above.

2. Claims 19 and 22 are rejected under 35 U.S.C. §103 as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook in view of the Aldrich Catalog.

Applicants note that claim 19 was previously addressed and that this rejection focuses primarily on claim 22, depending from claim 19.

Claims 1, 3, 19, and 24 are rejected under 35 U.S.C. §103 as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook in view of Utermohlen (U.S. Patent No. 5,437,976).

Claims 1 and 11 are rejected under 35 U.S.C. §103 as being unpatentable over Colpan et al. (U.S. Patent No. 6,383,393B1) in view of Sambrook in further view of Crossway (U.S. Patent No. 4,996,144). Applicants note that claim 1 was previously addressed and that the rejection focuses primarily on claim 11, depending from claim 1. Applicants respectfully traverse all the above rejections.

The arguments and remarks provided above are also fully relevant here and are incorporated by reference to avoid repetition. To briefly summarize, the combination of Colpan and Sambrook fails to teach all the elements of claims 1 and 19. Specifically, neither Colpan nor Sambrook, either alone or in combination, discloses contacting an RNA isolation membrane with an RNA-containing precipitate, where the membrane is a polymeric membrane and acts as a physical barrier to the RNA-containing precipitate and retains the RNA-containing precipitate for purification.

The tertiary references Aldrich (glass wool fibers), Utermohlen (affinity chromatography of nucleic acids using multi-functional oligos to bind molecules of interest) and Crossway (purification of dissolved nucleic acids by DNase treatment and solvent extraction) fail to remedy the shortcomings of Colpan and Sambrook.

Applicants assert that Sambrook and Colpan, taken alone, or in combination with each other, or in combination with the tertiary references cited, fail to teach all the limitations of the present claims. Therefore, the Examiner has not established a *prima facie* case of obviousness and the Applicants respectfully request withdrawal of the rejection and reconsideration of the claims in view of the amendments to the claims and remarks presented above.

Provisional Obviousness-type Double Patenting

Claims 1-3 are provisionally rejected for nonstatutory obviousness-type double patenting over claims 1-3 of copending Application No. 10/804,938 in view of Colpan.

Claims 19-22 are provisionally rejected for nonstatutory obviousness-type double patenting over claims 1-3 of copending Application No. 10/914,920 in view of Sambrook.

Without acquiescing to the above rejections, Applicants defer entry of a terminal disclaimer, if determined necessary, to a time when either the present application or one of the above applications has allowable claims.

Favorable consideration and entry of these amendments are respectfully requested. The Examiner is encouraged to contact the undersigned attorney with any questions regarding this application.

Respectfully submitted,
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Date: June 15, 2006

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**COPY OF
PRELIMINARY AMENDMENT
FILED NOVEMBER 26, 2003**

**ACCOMPANYING
JUNE 15, 2006
AMENDMENT AND RESPONSE IN
SERIAL NO. 10/693,428**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED
CENTRAL FAX CENTER
JUN 15 2006

Applicant: Robbins, C.A., et al.)
Serial No.: TBD)
Filed: October 24, 2003)
Title: Devices and Methods for)
Isolating RNA)
Docket No.: 29830-109CIP)

Art Unit: TBD
Examiner: TBD

BOX NON-FEE AMENDMENT
Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING (37.C.F.R. 1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: BOX NON-FEE AMENDMENT, Assistant Commissioner for Patents, Washington, D.C. 20231 on the date set forth below.

11/26/03
date of mail deposit

By:


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PRELIMINARY AMENDMENT

Sir:

In order to more correctly define the relationship of this application to U.S. patent application serial no. 10/631,189, filed on July 31, 2003, Applicants file the following amendment.

Status of claims:

Claims 1-27 (original)

Amendment to the Specification:

Please replace the paragraph "RELATED APPLICATIONS" with the following:

RELATED APPLICATIONS

This application is a continuation-in-part of and claims the benefit to U.S. patent application U.S. Serial No. 10/631,189, filed on July 31, 2003.

The above amendment is made only to more clearly define the lineage of the present application. The status of claims remain unchanged as of the filing of this application. No new matter has been added as a result of the above amendment.

The Examiner is invited to call the undersigned attorney at (617) 854-4237 should he determine that a telephonic interview would expedite prosecution of this case.

Respectfully submitted,



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Date: 6/26/03